October 25, 1949.

Dr. E. L. Tatum,
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California.

Dear Ed:

I will try to get W-757 and W-760 out again, and to you, as soon as possible. Thanks very much.

As far as recent advances in genetics go, things are decidedly lukewarm in this lab. The heterozygous diploids are probably old-hat by now, but maybe it would help to mention that Zelle has done innumerable single cell isolations on them, which just about clinch the notion of a sexual stage. The point is that, except for Mal, and a couple of nearby loci, the heterozygous cells split off , usually, either of the parental combinations of characters. There is some crossing-over, but the parental combinations are much more frequent. The parental groupings of factors are therefore intact, together, in the same cell. I still don't have the whole story on the "elimination mechanism" which causes the haplogenicity of Mal, S^r, etc.., in the diploids. Cavalli's Hfr strains have pretty well blown up, at least for our purposes— the recombination frequency is undoubtedly higher, but not high enough to pick recombinants without selection (conscious or otherwise!) Esther is doing some work on lambda now, to try to explain why we can recover a substantial proportion of lambda-negative prototrophs in crosses of lambda-positive and lambda-negative parents. It may be that the zygote becomes disinfected, and in the diploid condition may be more difficult to be made lysogenic. This would explain the cropping up of plaques in previously unblemished cultures of Salmonella when they are crossed and the prototrophs examined.

Lately, two recombining strains (+ K-12) have been found— at least they are very likely. One is in Salmonella coli 1; the other is another E. coli strain, from chickens. The situation is confused by the fact that reverted prototrophs can be selected from good double mutants(!) in some cases. I don't understand thisphenomenon at all, unless we happen to be hitting a common suppressor mutation (e.g. for threonine and histidine). But we also have reassortment of unselected markers which make it almost certainly recombination. So sex is not an isolated phenomenon.

I also spent some time to clean up the use of drug-resistance to select recombinants. The parents have to be grown together for a few hours/

but otherwise the results are quite straightforward. Streptomycin (100 u/ml) x azide (M/500), in nutrient agar, have worked best so far, although the Az^r mutation is frequent enough to cause a little trouble. Resistance, together with unselected markers, may be a method of choice for organisms with a finicky nutrition, ar which don't readily give mutants.

Miss Ethelyn Lively has been getting along well in a cytological study of diploids vs. haploids. There are some definite peculiarities, whose significamce re diploidy is not yet clear.

We were very glad to see the linkage data on Neurospora published from your group and Beadle's. But why the dickens isn't someone studying crossing-over? Or is someone?

With best regards,

Sincerely,

Joshua Lederberg